REMARKS

Entry of the foregoing, and further and favorable reconsideration of the subject application are respectfully requested.

Status of Claims

By the present amendment, claims 74-88, added in the amendment filed October 13, 2009, have been renumbered as claims 78-92. Claims 79-92 have been amended to correct their dependency. Claim 78 has been amended to recite that the mammal is suspected of suffering from cerebral ischemia which "affects glia or other non-cholinergic cells." Claim 78 has also been amended to recite that the IGF or analogue is administered "to the CNS" of the mammal. These amendments derive support from throughout the specification and claims as originally filed. Claim 80 has been canceled without prejudice to or disclaimer of the subject matter contained therein. New claims 93-96 correspond to previously deleted claims 64-65, 68-71, and 74-77. No new matter has been added.

Interview Summary

Applicants gratefully acknowledge the courtesy shown to their undersigned representative by the Examiner in the telephonic interview held December 18, 2009. In the interview, the rejections of the claims under 35 USC 103 were discussed. The Examiner indicated his willingness to consider a declaration in support of the patentability of the claims. The Examiner also noted that several of the now-canceled claims were not rejected on the basis of prior art or interference estoppel.

Objections under 37 CFR 1.172(a)

At pages 3-4 of the Official Action, the Examiner asserts that the application is not in compliance with 37 CFR 1.172(a), because the assignee has purportedly "not established its ownership interest in the patent for which reissue is being requested." Applicants respectfully disagree.

There are two inventors of the instant application: Peter Gluckman, and Karoly Nkolics. At the time the Statements under 37 CFR 3.37(b) were filed on November 1, 2004, Dr. Nickolicks had assigned his rights to Genentech, Inc. (Reel/Frame 015617/0156), while Dr. Gluckman had assigned his rights to Auckland Uniservices Ltd. (Reel/Frame 015618/0583). As each inventor is a joint owner of the patent, each inventor owns an undivided 100% interest in the patent. 35 USC 262. *See, MPEP 301.*

Since that time, Auckland Uniservices assigned its rights to NeuronZ Ltd. (Reel/Frame 015612/0905). In 2004, NeuronZ Ltd. was acquired by Neuren Pharmaceuticals, Ltd. (see attached Appendix 4E to Neuren's 2004 Preliminary Final Report). In 2007, Neuren Pharmaceuticals, Ltd. assigned its rights in the application to Genentech (Reel/Frame 019110/0928). Accordingly, Genentech is currently the sole assignee/owner of the instant application.

Rejections under 35 USC 251

Claims 78-92 stand rejected under 35 USC 251 as impermissibly broadened over the claims of U.S. Patent 5,714,460. Applicant maintains that the newly added claims are not broader than any of the original claims of the '460 patent in any respect. Accordingly, they

comply fully with 35 USC §251, and this rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

At page 5 of the Official Action, the Examiner argues that the recitation in the instant claims of "identifying an animal suspected of suffering from cerebral ischemia" represents an impermissible broadening of subject matter. The basis for the Examiner's argument appears to be that because

> a mammal can be suspected of suffering from cerebral ischemia without actually suffering from cerebral ischemia, e.g., because of the result of a faulty diagnosis or because of the result of a preliminary diagnosis based upon insufficient information, the instant claims embrace the treatment of mammals not embraced by the patent claims, i.e. of mammals suspected of but not actually suffering from cerebral ischemia.

In other words, the Examiner's position is that the new claims cover treatment of mammals that are mistakenly suspected of suffering from cerebral ischemia, while the patent claims do not. Applicants respectfully disagree with the Examiner's reasoning. During patent examination, the pending claims must be given their broadest *reasonable* interpretation consistent with the specification. *See, MPEP 2111.* Applicants submit that it is not *reasonable* to interpret the claims as covering treatment of mammals that are not suffering from cerebral ischemia, or to require absolute certainty on the part of the diagnostician. The only way to be absolutely certain that a mammal has suffered from cerebral ischemia is to examine its brain postmortem, at which point treatment of that ischemia is pointless. The patent claims do not require absolute certainty in diagnosis; indeed, the patent claims do not include a step of identifying a mammal suffering from cerebral ischemia at all. Accordingly, because the instant claims add the step of identifying a mammal suffering from cerebral ischemia, they are necessarily *narrower* than the patent claims, as it is axiomatic that adding limitations narrows claims.

The Examiner further argues that the instant claims are broader than the patent claims because "the patent claims require a CNS insult which affects glia or other non-cholinergic cells" while the instant claims do not. Without conceding to the Examiner's argument, but solely in an effort to expedite prosecution, the instant claims have been amended to recite ischemia which affects glia or other non-cholinergic cells.

Finally, the Examiner argues that the instant claims are broader than the patent claims because "the patent claims require the IGF-1 or biologically active analogue thereof to be administered to the central nervous system of the mammal, whereas the instant claims only require the IGF-1 or biologically active analogue thereof to be administered to the mammal, and not to any particular location in the mammal." Without conceding to the Examiner's argument, but solely in an effort to expedite prosecution, the instant claims have been amended to recite that the IGF-1 or biologically active analogue thereof is administered to the CNS of the mammal.

Claims 78-92 also stand rejected under 35 USC 251 as purportedly based on new matter. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

The Examiner argues, at p. 6 of the Official Action, that the claimed "step of identifying a mammal suspected of suffering from cerebral ischemia is new matter." According to the Examiner, the specification does not teach an "identifying step and does not recite mammals which are 'suspected' of suffering from cerebral ischemia." Applicants respectfully disagree. At column 1, lines 20-60, the specification discusses a number of diseases and injuries associated with cerebral ischemia, including, perinatal asphyxia, near miss drowning, carbon monoxide inhalation, cardiac arrest, hypotensive episodes and hypertensive crises. As noted above, the claims are to be given their broadest *reasonable* construction consistent with the specification, and the specification clearly contemplates treating patients suffering from conditions that are

known to be associated with cerebral ischemia. A patient suffering from, for example, carbon monoxide inhalation, would reasonably be *suspected* of suffering from cerebral ischemia, and would reasonably be treated using the claimed methods, without taking the step of removing the patient's brain to confirm that cerebral ischemia had, in fact, occurred. It is true that Example 1 discusses treatment of an animal known to be suffering from cerebral ischemia; this is confirmed in the Example by the use of a control group, and by histological examination of the brains of the subjects postmortem. However, postmortem histological examination of a patient's central nervous system is neither recited in the claims, nor required by the teachings of the specification.

The Examiner further argues, at page 6 of the Official Action, that the dosage range and the calculation of dosage based upon brain weight of the mammal recited in new claim 80 is new matter. Without conceding to the Examiner's argument, but solely in an effort to expedite prosecution, claim 80 has been canceled without prejudice or disclaimer.

The Examiner further argues, at page 6 of the Official Action, that the "recitation of intrathecal and epidural administration, or of administration by the cerebral vasculature or via the carotid artery… is new matter." Applicants respectfully disagree. The specification recites, at col. 5, lines 45-50, that the claimed compositions "may be administered directly into the brain *or cerebrospinal fluid* by techniques including lateral ventricular through a burrhole or anterior fontanelle, *lumbar or cisternal puncture or the like.*" (Emphasis added). One of ordinary skill in the art would understand that administration via "lumbar or cisternal puncture" accesses the cerebrospinal fluid (*see, e.g., http://www.nlm.nih.gov/medlineplus/ency/article/003428.*htm), as does intrathecal or epidural administration, and thus would interpret the disclosure of "lumbar or cisternal puncture *or the like*" to encompass other well-known methods of spinal administration to the CSF, such as intrathecal and epidural administration. Likewise, the specification teaches

at col. 5, lines 43-46, that "IGF-1, analogues thereof...can be administered centrally or systemically. Desirably, the compositions are administered directly to the CNS of the patient." One of ordinary skill in the art would understand that "systemic" administration encompasses intravenous administration, and that administration via the cerebral vasculature, or via the carotid artery, accomplishes the desired result of administration to the CNS.

Finally, the Examiner argues that the recitation of "asphyxia, trauma, embolism, thromboembolism, and toxin" introduces new matter into the claims. However, these disorders are clearly and explicitly disclosed at col. 1, lines 44-61 of the patent.

Rejections under 35 USC 112, ¶1

Claims 78-92 stand rejected under 35 USC 112, ¶1 as purportedly unsupported by an adequate written description in the specification. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed, for the reasons discussed above with respect to the rejections of the claims under 35 USC 251.

Rejections under 35 USC 103

Claims 78-92 stand rejected under 35 USC 103 as purportedly estopped on the merits by the final judgment in interference No. 104,533; and as purportedly obvious over WO90/14838 and over Gluckman et al. *Biochem Biophys Res Comm* 182:593-599. These rejections, to the extent that it applies to the claims as amended, are respectfully traversed.

Hypothermia is known in the art to offer protection from the damage associated with ischemic stroke. *See, e.g.,* Krieger, Derk. et al."Cooling for Acute Ischemic Brain Damage." American Heart Association. May 25, 2001, pg. 1847-1854; Schwab, S. et al. "Moderate

Hypothermia in the Treatment of Patients with Severe Middle Cerebral Artery Infarction." American Heart Association. July 31, 1998, pg. 2461-2466, Florian, et al. (2008). "Long-term hypothermia reduces infarct volume in aged rats after focal ischemia". *Neuroscience Letters* **438**: 180–185. Jess, et al. (2009). "Review Article of the Use of Early Hypothermia in the Treatment of Traumatic Brain Injuries". *JSOM Summer 2009 Volume 10 Edition 1* **10**. However, the present inventors have surprisingly found that IGF-1 can prevent the damage associated with ischemia when injected in volumes which do not alter brain temperature. This is not simply a question of dose optimization. Prior to the inventors' discovery that IGF-1 had the capacity of preventing the damage caused by ischemia without altering CNS temperature, one of ordinary skill in the art would have been motivated to administer IGF-1 in volumes which decreased CNS temperature, in order to maximize the cooling protective effect. However, with the knowledge provided by the present inventors, it is advantageously possible to effectively administer IGF-1 in low volume doses, as the cooling effect provided by the lower concentration/higher volume dose is not necessary. This means that the neuro-protective effective is provided by IgF-1 irrespective of any cooling effect. This feature is neither taught nor suggested by the prior art, and is not inherent in the high volume doses taught in the prior art. As a result, the present claims are patentably distinct from the cited art, and are not estopped by the judgment in interference 104,533.

Conclusion

In the event that there are any questions concerning this paper, or the application in general, the Examiner is respectfully urged to telephone Applicants' undersigned representative so that prosecution of the application may be expedited.

The Commissioner is hereby authorized to charge any insufficient fees or credit any overpayment associated with this application to Deposit Account No. 50-4047 (7046529001).

Respectfully submitted,
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